

REMARKS

With entry of the amendment, claims 51-61 are pending; claims 1-50 are cancelled without prejudice or disclaimer. Claims 37-50 were under consideration, and were rejected, as summarized below.

Newly added claims 51-61 are fully supported by the specification and introduce no new matter. Claims 51-61 are directed to a method of detecting a nucleic acid sequence in a sample and recite, among other things, the specific nature of the anthraquinone quencher used in the method. In independent claim 51, the steps of the method are recited. Support for these steps is found throughout the specification but at least at paragraphs [0043], [0048], [0051], [0052] and [0053]. The anthraquinone quenchers recited in the claims quench via energy transfer or ground state quenching. Support for this mechanism is found through out the specification and at least specifically in paragraphs [0003], [0004], [0051] and [0053]. Claim 51 recites that the anthraquinone quencher is an α -aminoanthraquinone. This is at least supported by formula (1) wherein an α -position is amino substituted. It is noted that the α and β position nomenclature is the conventional designation for the carbon positions around the tricyclic anthraquinone structure relative to the keto groups of the center ring. Due to the symmetry of the anthraquinone molecule, there are four equivalent α positions and four equivalent β positions.

With respect to claim 52, support is found at least in formula (1) and paragraph [0020]. Support for claim 53 is found at least in paragraph [0018]. Support for claim 54 can be found at least at formulas (1), (1a), (3') and paragraph [0023]. Support for claim 55 can be found at least at formulas (1), (1a), (3') and paragraphs [0068] and [0070]. Support for claim 56 can be found at least at paragraphs [0051] and [0052]. Support for claim 57 can be found at least at paragraph [0004]. Support for claim 58 can be found at least at paragraphs [0003] and [0004]. Support for claim 59 can be found at least at paragraph [0054]. Support for claim 60 can be found at least at paragraphs [0052], [0053], [0057], and Example 17. Support for claim 61 can be found at least at paragraphs [0052], [00533], [0057], and [0058].

The specification has been amended to correct a typographical error and to correct the proper name for "FRET." No new matter is added by this amendment.

The cancellation of claims is not intended to be a dedication to the public of the subject matter canceled. Applicants reserve the right to file a continuation application directed to the canceled subject matter.

Acknowledgement

Applicants wish to thank Examiner Staples, Primary Examiner Strzeleck, and Supervisor Benzon for the opportunity to discuss, in an April 28, 2009 in-person interview, the presently claimed invention and to explain how it is patentable over the prior art.

Rejection of claims 37-50 under 35 USC §102

Claims 37-40 were rejected under 35 USC 102(e) as being anticipated by Jones et al. (US Patent No. 7,122,383). Applicants reserve the right to antedate Jones et al. Without acquiescing to the merits of this rejection, the rejection is rendered moot by cancellation of claims 37-40.

To the extent that Jones et al. may be properly applied against the currently pending claims 51-61, applicants respectfully point out that Jones et al. fails to teach a method that employs an oligonucleotide labeled with a fluorophore and an α -aminoanthraquinone quencher. Therefore, Jones et al. does not anticipate any of claims 51-61.

Rejection of claims 37-50 under 35 USC §103

Claims 37-47, 49, and 50 were rejected as being unpatentable over Ju et al. (PNAS 92:4347-4351, 1995), Batz et al. (US Patent No. 6,117,973), and Schuster (Acc. Chem. Res. 33:253-260, 2000). Claims 37-47, 49 and 50 have been canceled, and therefore, this rejection is moot as to those claims.

To the extent that this combination of references is applicable to the currently pending claims, applicants discuss the combination as follows.

Ju et al. discloses fluorescence energy transfer dye-labeled primers for DNA sequencing. The Examiner acknowledges that Ju et al. do not disclose anthraquinone quenchers.

Schuster reports a study of the mechanism by which anthraquinones causes DNA strand cleavage upon irradiation. One of the anthraquinones employed, AQA, was modified in a β position with an amide linked through its nitrogen atom (p. 253, column 2). This anthraquinone, which was not covalently bound to the DNA but rather, associated with the DNA by intercalation, caused cleavage of the DNA following irradiation, which Schuster concluded could only be possible if the reaction occurred by electron transfer (p. 254, column 1, second full paragraph). Further, the Examiner acknowledges that Schuster does not teach anthraquinone quenchers.

Batz et al. pertains generally to detecting nucleic acid in a sample by detecting transfer of an electron or an electron hole between an electron donor and an electron acceptor. One class of compounds disclosed as potential electron acceptors is modified anthraquinones. Claim 7 is directed to a genus of anthraquinones that encompasses millions of compounds, including, arguably, an α -aminoanthraquinone. However, Batz does not show any examples of nor provide any guidance to select an α -aminoanthraquinone, as is required by claim 51.

Further, Batz et al. teaches away from the use of fluorescence quenching by energy transfer, as opposed to electron transfer. At column 21, lines 55-59, Batz states:

The ideal fluorescer will have the energetics so that energy transfer to the anthraquinone is impossible but electron transfer is fast.

At column 21, lines 52-54, Batz discusses:

... things can be done to improve the [electron transfer] system: (i) A more easily-oxidized (reduced) donor (acceptor)

In other words, Batz teaches that the system can be improved by using a more easily reduced acceptor to increase electron transfer rate. Clearly, a key aspect of the invention disclosed by Batz et al. is inconsistent with the use of a quencher that reduces fluorescence by energy transfer or ground state quenching, as recited, e.g., in claim 51. Further, one of skill in the art would not have been motivated to select from among the millions of compounds encompassed by claim 7 an anthraquinone modified to include an α -amino group, which would make the anthraquinone less easily reduced, and thus, lead to decreased electron transfer rates.

Energy transfer quenching and ground state quenching are distinct from electron transfer quenching. The Batz reference itself makes a clear distinction between these two mechanisms, and teaches, at column 36, line 10, that electron transfer is preferable because the particular choice of donor and acceptor is not so limited:

“The choice of electron transfer rather than energy transfer in the present invention arises from the fact that fewer restrictions are placed on the donor and acceptor moieties for photoinduced electron transfer...”

Furthermore, in contrast to energy transfer and ground state quenching, electron transfer quenching causes the formation of a new chemical species, which, in the case of anthraquinone electron transfer quenchers, is a radical anion. Radical anions are a highly reactive species that can damage DNA and cause strand scission (see, for example, Schuster). Applicants' discovery


that substitution of an α -position of an anthraquinone with an amino group results in α -amino anthraquinone that quenches by energy transfer or ground state quenching was thus completely unexpected and surprising.

Claim 48 was rejected as being unpatentable over Ju et al., Batz et al., Schuster, and Jenne (US Patent No. 6,4551,535). Claim 48 has been cancelled, rendering moot the rejection. The Jenne et al. reference, which is cited as teaching a method of measuring RNase activity, is not relevant to the pending claims, nor does it cure the deficiencies of the cited references. Moreover, the Examiner acknowledges that Jenne et al. does not teach anthraquinone quenchers.

Applicants believe that the present application is in condition for allowance. Favorable reconsideration of the application is respectfully requested. Should any questions remain, the Examiner is encouraged to contact the undersigned at **608.257.3501** so that prompt disposition of the application may be achieved.

Please charge the extension fee to Deposit Account No. **50-0842**. No other fee is believed due in connection with this submission. However, the Commissioner is authorized to charge any other fee which may be required to Deposit Account No. **50-0842**.

Respectfully submitted,



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